Standardization of Clinical Decision Making for the Conduct of Credible Clinical Research in Complicated Medical Environments

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ABSTRACT

The likelihood that past experience will produce correct guides to current practice depends on the signal-to-noise ratio for the clinical problem of interest. If the signal-to-noise ratio is high, the decision will be sound and patient benefit likely to occur. If the signal-to-noise ratio is low, as is commonly the case with difficult clinical decisions, then personal experience and the best intentions will not assure sound clinical decisions. When the probability of benefit cannot be quantified, clinicians in complex settings are in danger of being misled by data and experience. Quantifiable probabilities established by group experiment or observation will be necessary for clinical decisions that can be expected to confer benefit on the patient. Explicit methods are necessary for interventions that can be replicated in experiments or in practice. Computerized protocols force the articulation of explicit clinical care methods and standardize clinical decision making. We have developed explicit, rule-based protocols, implemented them in our hospital, exported them to other hospitals, and successfully achieved a rigorous experimental environment in the clinical ICU. Exportation of such explicit methods may narrow the gap between efficacy (university hospital) and effectiveness (community hospital) research results.

INTRODUCTION

Medicine is and has traditionally been an empiric undertaking [1-5], based, therefore, on experience, including experimentation. The scientific rigor of the empiric observation is the key concern. Experimental method figures prominently in the evaluation of scientific rigor. The randomized clinical trial (RCT) is widely regarded as the most rigorous clinical investigative method for therapy evaluation [6-14]. The Cardiac Arrythmia Suppression Trial provides a striking example of the value of an empiric RCT, the results of which reversed standard practice that had been securely based on extensive pathophysiologic understanding [15, 16]. It is only one of many therapies initially enthusiastically embraced and widely applied, only to be abandoned when rigorous studies revealed them to be useless or even harmful [9, 12]. Since clinicians can easily be misled by experience, rigorous evaluations of critical care interventions should be pursued and should be made the basis of practice guidelines.

Reproducibility (replication of results by different investigators) is a key requirement of new information before it becomes incorporated into the body of accepted scientific knowledge [12, 17, 18]. Replication of scientific work can only take place if the original method is explicit. Without clear articulation of essential methodologic details, it is not possible to reproduce a clinical study. Because of the multiple variables that may influence the outcome of critically ill patients, the challenge of articulating an explicit method in adequate detail is daunting, but it is achievable [19-21]. The demanding task of assuring the consistent implementation of the method by clinicians in the unpredictable clinical setting is even more challenging.

Two major elements, the patient and the clinical caregiver, determine the intensity of patient care and the patient outcome. Both the patient and the clinical caregiver are sources of random noise and of systematic noise (bias). The patient contributes noise because of uncontrollable host factors and because of disease etiology, severity, extent, and duration. Local factors influence the patient's disease and the spectrum of clinical problems. The patient identification and selection process is quite imperfect and may incorporate much local bias due to the prejudices of individual clinicians and investigators. This bias is the result of many factors, among which are characteristics of local clinical environments and failure of the medical community to establish broadly accepted specific definitions of many diseases [22, 23]. The clinical caregiver response to the patient also introduces both random noise and bias. Bias is injected into the response of clinical caregivers because of strongly held opinions based on many factors that influence behavior, including general and local cultural factors, local technical abilities, background, training, and experience. These biases can be important non-experimental co-interventions. They can influence patient outcome and confound the interpretation of clinical trial results leading to inappropriate inferences about the effect of experimental interventions.

The detection of an association between an input signal of interest and an outcome measure requires that the signal of interest be capable of separation from other, unwanted, signals with which it may be confused or by which it may be obscured. A common measure of this capability is the signal-to-noise ratio. Unless the signal-to-noise ratio exceeds 1, the signal will be undetectable. For interventions with large signal-to-noise ratios, uncontrolled observations or small clinical trials can be definitive (e.g., the introduction of penicillin for pneumococcal

0195—4210/96/$5.00 © 1996 AMIA, Inc.

pneumonia, or lemon juice for scurvy [24]). However, for clinical with low signal-to-noise ratios, uncontrolled observations may be misleading [25].

The internal validity of clinical trials requires equal treatment of the study groups [9, 27 and 28 in 18, 26]). Non-double-blinded studies must be scrutinized for comparability of the non-investigative co-interventions in the experimental treatment arms. However, many interventional critical care studies, including those that incorporate mechanical ventilation techniques, cannot be double-blinded. In these situations particularly, process control, standardization of clinical decision making, and control of the clinical environment become important in establishing the clinical environment as a clinical laboratory equal to the task of conducting the requisite systematic observations under rigorous experimental conditions. The use of point-of-care decision support tools to standardize clinical decision making (achieve process control) is effective and promising, but not widely available [25, 29, 30].

STANDARDIZED DECISIONS

Since treatments must be applied in a uniform manner to comparable patients before one can evaluate the outcome of a particular medical intervention, the standardization of clinical decision making is of importance [12]. Virtually all clinical trials employ protocols. These protocols include definitions, patient selection criteria, procedural rules, and guidelines for conduct of the trial. They generally provide some specific instructions, but they are not specific enough to adequately control the moment-to-moment process of care. Algorithms usually contain non-specific, judgment-requiring suggestions like "optimize PEEP" or "maximize antibiotic therapy. Clinical algorithm texts and other published guidelines also contain many such general instructions [31-35]. While general instructions provide guidelines and are of value for their conceptual content, they are not executable and fail to standardize clinical decision making. The application of general guidelines is associated with great variation of practice by different clinicians, due to variation in individual clinical practice styles.

Control, measurement, and analysis are the cardinal features of rigorous clinical investigation [36]. Of the three elements, it is control that is usually lacking in the clinical environment with the result that unnecessary variation in clinical care characterizes most critical care clinical trial research [37]. This may result in decreased signal-to-noise ratio for clinical outcomes [25, 38]. The lack of control of clinical care processes may explain much of our failure to define the impact of ICU therapies.

Traditional laboratory research is well know for its control. The misperception that laboratory level control is impossible to achieve in the clinical ICU environment is widespread. This misperception itself is an important determinant of the clinical research programs mounted in the medical community. It constitutes a paradigmatic view that limits the possibilities for clinical research [4, 5]. The traditional expert (authoritarian) clinical decision making paradigm is based on the incorporation of a large number of current variable values. These are assessed with published information and past physician experience and adjusted for the individual patient [39]. Humans are limited in ability to deal with extensive information. Since many clinical therapeutic decisions made in the complex ICU environment are strongly influenced by items recalled from memory, it is appropriate to question both the suitability of this traditional decision making process and the belief in its superiority over more consistent actuarial (data and rule based) decision techniques [29, 40-58]. A serious reassessment of the widespread clinical belief in the impossibility of *control* in the ICU for both clinical and research processes is needed.

Computerized protocols are an effective way to eliminate unnecessary variation in clinical care and thus impose control on the clinical care process [29]. This control can be expected to reduce noise introduced by the clinical caregiver and increase the signal-to-noise ratio for ultimate clinical outcomes [20, 21, 39, 59]. Humans require support for the persistent commitment to detail and to decision making logic (rules) necessary to generate consistent and reproducible clinical decisions.

PROTOCOL RESULTS

Protocols developed and refined at the LDS Hospital, using the hospital-wide HELP system [60-62], have been exported to PC (Unix and Quinix) platforms and used by other clinical centers in a randomized clinical trial of Acute Respiratory Distress Syndrome (ARDS) patients (AHCPR: HS06594, T. D. East, Ph.D., Principal Investigator). The outcomes of two groups, one with mechanical ventilation clinical decisions standardized with bedside computerized protocols, and the other with mechanical ventilation decisions made exclusively by clinicians, are being compared. About 100 patients have been randomized in 9 centers. Preliminary data analysis indicates a performance during 24,000 hours of application in these 9 centers that is indistinguishable from that at the LDS Hospital where the protocols were developed and where standardized clinical decision making occurred 95% of the 24 hour day in about 100,000 hours of around-the-clock use in about 250 ARDS patients .

There is a natural concern about possible harmful effects of protocol standardized clinical decision making. Data do not support this concern. Patients with ARDS who are supported with computerized protocols have experienced a higher survival than expected from historical control data [29]. However, there are no data supporting a causal association between computerized protocol use and patient outcome. In fact, from 1987 to 1991 at the LDS Hospital the same unexpectedly high survival was observed in ARDS patients supported with or without computerized protocols that provide decision support for mechanical ventilation [63], and a higher survival during the same period has been reported from the Specialized Center of Research in ARDS at the University of Washington [64]. Computerized protocol decision support of mechanical ventilation appears feasible, safe, and practical (given an appropriate clinical computer infrastructure), but its impact on patient outcome is only currently being explored. Other randomized clinical trials, using less detailed and manually applied protocols, have demonstrated clearly that protocol guided care favorably affects the outcome of patients with thromboembolic disease [65-67].

SUMMARY

The likelihood that past experience will produce correct guides to current practice depends on the signal-to-noise ratio for the clinical problem of interest. If the signal-to-noise ratio is high, the decision will be sound (the strength of inference will be high) and patient benefit likely occur. If the signal-to-noise ratio is low, as is commonly the case with difficult clinical decisions, then the strength of inference will be low and personal experience and the best intentions will not suffice. The quantifiable probabilities established by randomized clinical trials will be necessary for clinical decisions that can be expected to confer benefit on the patient. When the probability of benefit cannot be quantified, clinicians in complex settings are in danger of being mislead by data and experience. Computerized protocols standardize clinical decision making. They force the articulation of explicit clinical care methods.

We have developed explicit, rule-based protocols, implemented them in our hospital, exported them to other hospitals, and successfully achieved a rigorous experimental environment in the clinical ICU. Exportation of such explicit methods may narrow the gap between efficacy and effectiveness research results.

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Acknowledgements: This work was supported by NHLBI grant #HL36787, AHCPR grant #HS06594, the Respiratory Distress Syndrome Foundation and the Deseret Foundation (LDS Hospital).